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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,790	08/10/2001	Bassil I Dahiyat	A-67229-9/RFT/RMS/RMK	6955

7590 09/26/2003

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EXAMINER

WESSENDORF, TERESA D

ART UNIT

PAPER NUMBER

1639

DATE MAILED: 09/26/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicant No .	Applicant(s)
	09/927,790	DAHIYAT ET AL.
Examiner	Art Unit	
T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 05 June 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,3 and 10-18 is/are pending in the application.
 - 4a) Of the above claim(s) 10-18 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1 and 3 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>15</u> .	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

Election/Restrictions

Response to Arguments

Applicant's arguments with respect to the submitted claims 10-18 as being withdrawn since they are independent or distinct from the elected invention have been fully considered but they are not persuasive.

Applicants argue that the claimed subject in each group is related by a commonality of operation, function and effect. It is further argued that MPEP 803 states that if the search and examination of the entire application can be made without serious burden, then the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

In response, the claimed subject of the newly submitted claims do not contain a common operation in that the newly submitted claims contain limitations such as the probability distribution of amino acids in a plurality of variant positions. Thus, examining these additional limitations would indeed pose undue burden of examinations i.e., with respect to the different statutes.

Status of Claims

Claims 2 and 4-9 have been cancelled in the Amendment of 1/23/03. Claims 10-18 are added in the current amendment.

Claims 10-18 are withdrawn from consideration, for reasons set forth above.

Claims 1 and 3 are under examination.

Specification

The objection to the disclosure because of the embedded hyperlink is withdrawn in view of the amendments to the specification.

The objection with respect to the incorporation of essential material in the specification is withdrawn in view of applicants' arguments.

Claim Rejections - 35 USC § 101

Claims 1 and 3 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility for reasons set forth in the last Office action.

Response to Arguments

Applicants argue that the instant invention provides a method for computationally screening variant protein sequence libraries to generate secondary libraries of useful variant protein sequences, which when synthesized find use in a wide

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variety of applications, ranging from industrial to pharmacological uses. It is further argued that the methodology allows for the rapid screening of large numbers of potential variant sequences for useful variants and the selection of proteins with useful properties.

In response, applicants' arguments are not commensurate in scope with the claims. The claims do not recite for a computationally screening of libraries. Furthermore, as evident from applicants' arguments, the wide application to an industrial and pharmacological use is not the specific and well-established utility mandated by the statute.

Applicants draw the examiner's attention to the Utility Guidelines and cite *In re Langer*. It is argued that *Langer* and subsequent cases direct the Patent Office to presume that a statement of utility made by an applicant is true.

In response, it is not whether the utility is considered true or not. Rather, whether the utility is specific and well established. *In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed

compound in terms of **possible use so general as to be meaningless** and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.') (Emphasis ours).

The instant claim methods provide for generating a secondary library of as yet undetermined structure, function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the secondary library was, as of the filing date, useful for any industrial or any pharmacological uses, as argued. Until some actual and specific significance can be attributed to the secondary library or even the compounds present in the library, an artisan would be required to perform additional experimentation in order to determine how to use the generated secondary library. Thus, there was no immediately apparent or "real world" utility as of the filing date.

Because any potential pharmacological utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. The specification does not disclose any specific and substantial interpretation for the result, and none is known in

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the art. In order for generated library to be useful, as asserted, for any pharmacological use, there must be a well-established or disclosed correlation or relationship between the claimed library and a disease or disorder.

"Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its ***potential role as an object of use-testing.***" *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101. The evidence of record is inadequate to determine the disease(s), drug(s) for which the compounds would be useful. In *Brenner*, the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible compounds the utility of which has also not been identified. *Brenner*, 148 USPQ at 690. (Emphasis added).

Thus, the secondary library of as yet undefined structure allegedly generated from the claimed method does not have a real-world utility i.e., a specific and substantial or well-established utility.

Claims 1 and 3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes protein design using specific (computational) program design, does not reasonably provide enablement for any type of secondary library of scaffold protein variants or sequences because of the reasons advanced in the last Office action.

Response to Arguments

Applicants argue that a patent need not teach, and preferably omits, what is well known in the art. Applicants cite page 8, lines 16-19 and page 9, lines 13-20. Applicants further argue that with respect to the scope of the enabling disclosure not commensurate with the scope provided in the specification, there is a disclosure of using a computational design program, and preferably PDA technology.

In response, a review of the cited section provides a general scope as broad as the claimed method. It is not apparent from the disclosure or applicants' arguments as to the any other protein library, besides the enzyme, that has undergone mutations on the primary structure to create a primary library. And, subsequently the different mutations in the entire primary library that generates a secondary library. As applicants clearly stated, the specification provides for a disclosure that uses a computational design program, for which the broad claimed invention does not positively recite.

Applicants cite *In re Goffe* and *In re Angstadt*.

In response, Applicants are working in a field of chemistry where little prediction is possible and that scope of claims should not be unduly extensive in such fields where applicability is highly speculative or not explored. Applicants

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may not preempt an unduly large filed by the expedient of making broad prophetic statements in the specification and claims unless the accuracy of such statements is sufficiently supported by well-established chemical principles or by sufficient number of examples. The high unpredictability of the newly emerging biolibrary art is recognized by no less than applicants, specifically at page 1, lines 13-25 and page 6, line 3 up to page 7, line 3.

Accordingly, the enabling disclosure for an enzyme (which in itself covers a broad scope of protein enzymes) using computational method would not be enabling for any type of other proteins that can be generated from the broad method steps of undefined components or structures.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Response to Arguments

Applicants draw the examiner's attention as to the term filtered set at page 26, line 20 up to page 27, line 4. Filtered set as argued is used in the present application as the optimized protein sequences that are generated using some sort of ranking or scoring function.

In response, a review of the cited section reveals that a filtered set, in some cases, comprise an **arbitrary** or random selection of a subset of the primary sequences. In a preferred embodiment, the filtered set comprises a rank ordered list of sequences. [It is therefore suggested that a rank order list of sequences be used, instead of a filtered set].

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Fechteler et al (JMB).

Fechteler et al discloses a method of producing a secondary scaffold library from a primary comprising of indels. See e.g., page 118, Table 5. Fechteler et al further discloses at page 119 up to page 123, specifically Figure 7 HCAPD algorithm. See also the Methods at page 128 up to page 129. Accordingly, the specific method steps of Fechteler using specific components in the

detailed Methods fully meet the broad steps of the claimed method of undefined structural components.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,403,312. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed invention of a filtered set, read in the light of the specification is similar, if not the same, as the '312 patent method of producing a secondary scaffold library with a rank list order.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T.D.W
T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
September 22, 2003